Exhibit A

Accompanying the Amendment filed
June 5, 2009 in Application Serial No. 10/542,914

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Alfred MARCHAL

Appl. No. : 10/542,914

Filed : January 20, 2004

For : USE OF COMPOSITION COMPRISING VITAMIN K1 OXIDE OR A DERIVATIVE THEREOF FOR THE TREATMENT AND/ OR THE PREVENTION OF MAMMAL DERMATOLOGICAL LESIONS

Examiner : CHO, JENNIFER

Group Art Unit : 1621

DECLARATION UNDER 37 C.F.R § 1.132

Mail Stop Amendment

Commissioner for Patents
P O Box 1450
Alexandria, VA 22313-1450

Dear Sir:

1. This Declaration is being submitted to demonstrate that a composition as claimed and comprising Vitamin K1 oxide provides (compared to a composition comprising Vitamin K1) unexpected results in the treatment of mammal dermatological lesions.
2. I am an expert in the field of the invention and I am familiar with the specification and prosecution history of the present US Patent application.
3. I have extensive experience in the field of the claimed invention as indicated in the attached Curriculum Vitae provided herewith as Exhibit A.
4. A major drawback for patients undergoing invasive medical or surgical techniques for aesthetic improvement is the downtime needed before that can resume their social and professional activities. In this post-treatment phase, the bruising, redness and swelling are key concerns.

5. In the enclosed study, I have tested composition comprising Vitamin K and composition comprising Vitamin K oxide.

   Both creams have the same carrying composition except the active vitamin. The obtained data show that the composition comprising Vitamin K1 oxide is more effective in the treatment of post operative bruising.

6. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: 20 - 02 - 2007 By: _____

KARAVANI

Topical use of vitamine K versus vitamine K oxide: A clinical evaluation of postoperative bruising and oedema

Dr. med. I. Karavani et al.
Carpe Clinic, Antwerp, Belgium
www.carpe.be

Introduction

One of the major drawbacks for patients to undergo invasive medical or surgical techniques for aesthetic improvement is the downtime needed before they can resume their social and professional activities. In this post-treatment phase, the bruising, redness and swelling are major elements. Of all measures taken to reduce this discomfort, the new vitamin K oxide, a metabolite, is used in comparison to the vitamin K, already known for the reduction of bruising. It seems that the use of vitamin K oxide gel yields significantly less bruising than the vitamin K cream.

Objective

The goal of this study was to evaluate the effects of vitamin K cream versus vitamin K oxide cream in post-operative bruising. For this purpose the blepharoplasty of the upper eyelid, an intervention known for its major bruising, was chosen.

Pharmacological aspects

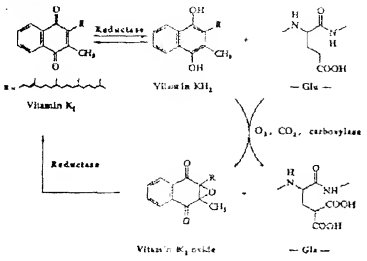
Vitamin K and vitamin K oxide

For some ten years now, more and more authors have published the results of their works concerning the interest of using vitamin K topically to prevent and treat various pathologies, other than the standard indications that have been known for a long time, such as hypo-prothrombinaemia and vitamin K deficiencies.
It is known that the metabolite pathway of vitamin K conducts to vitamin K oxide as the active metabolite, as described below (JAMCS, 1991, 113, 7734-7743).
Several studies (not all published) have shown that cosmetic creams containing vitamin K oxide are more active topically than cosmetic vitamin K cream.
Vitamin K oxide has many physico-chemical advantages over vitamin K in terms of a faster action for dermal indications, stability to light and heat, allergenicity, etc. These advantages are due to the stabilization by an oxygen atom of the very instable double bond in the naphtoquinone ring of the vitamin K molecule.

In this trial, we tested Auriderm K2 Gel (Vitamin K in nanosomes formula) versus Auriderm XO (vitamin K oxide in nanosomes formula.). Thus both creams have the same carrying composition except the active vitamins.
We have chosen the nanosomes vectors because of their best efficacy that was shown in previous studies (Delune, March 2001, J.Med.Esth.& Derm.XXVIII 109, and Batello, Belgium 2003).
The nanosomes, containing phospholipids, increase skin penetration and act as powerful vectors for these lipophilic substances.

Mechanism of Action of Vitamin K

Scheme I



Vitamin K or 2 methyl, 3 phytol 1-4 naphtoquinone, is a yellow vitamin, liposoluble, relatively viscous and odourless. Only the *trans* form is active. It is needed for the synthesis of prothrombin (factor II) and the coagulation factors VII, IX and X.
This substance is very sensitive to light.

Vitamin K oxide or 2 methyl -3- phytyl -1-4 naphtoquinone 2, 3 oxide is a colourless, viscous and odourless liposoluble liquid. This substance is not sensitive to light.

Indications

- Purpura caused by pulsed dye laser;
- All other forms of purpura (actinic, medicinal, spontaneous, traumatic);
- Pre- and post-sclerotherapy:
- Before and after all injections of wrinkle filling products;
- Erythema caused by laser CO2 resurfacing;
- Red blotches;
- Telangiectasias;
- Following aesthetic and plastic surgery bruises;
- Legs spider veins.

Action Mechanism

Recent literature makes it possible to understand better and better how vitamin K intervenes in the physio-pharmacology of the skin. The role of the Galenic appears vital. If the formulation contains vitamin K in its free form, i.e. not encapsulated in nanosomes, vitamin K being liposoluble will tend to dissolve in oil during the oily phase of the water emulsion.
Conversely, if the vitamin K is encapsulated in nanosomes, its migration through the epidermis will be highly facilitated and it will reach without problem the papillary and reticular dermis where its target is located. Vitamin K is highly sensitive to light and must be kept in a tube; this is not the case with the vitamin K oxide.

Conclusion

The most recent data provided on the use of topical vitamin K seem to confirm its value for the indications mentioned above.
The importance of the type of vehicle and the one of the Galenic are primordial to ensure the stability of the preparation.

Materials and methods

10 patients with redundant upper eyelid skin and fat pockets were selected for the trial. The operation was performed under local anaesthesia (5 cc of lidocaine 1% and adrenaline 1:80.000) combined with oral use of Atarax 25mg, Valtran 10 drops and an IM injection of 2.5 cc Dormicum.
Resection of the skin was done by radio-surgery (Ellman, Inc.); resection of a rim of the orbicularis muscle and the fat pockets was done with scissors and a CO2 laser. Coagulation before closure was performed with the Ellman bipolar mode.
After the intervention the patient was advised to rest with cold compresses with Terramycin cream. From the second day on, an "anti-bruising" gel was used. In this single blind evaluation the patients received two identical looking containers with gel of identical consistency. The gel for left side (marked by an L) contained the Auriderm K2 Gel, while the right side (marked by an R) contained the Auriderm XO. The gels were applied twice a day for four days. At the sixth day the stitches were removed and the bruising was evaluated by photography and a score from 0 to 5 (none, slight, moderate, major, exceptional, as seen in blood clotting disorders or persistent bleeding). Oedemas were evaluated with a similar score from 0 to 5.

The operation is quite invasive compared to regular treatments in an aesthetic clinic. The location on the face is an exposed region and known for extreme bruising. All these criteria make this operation to a reliable object for the evaluation of bruising.

Results

Despite the aggressive intervention on a delicate zone, there was moderate to minimal bruising and swelling on both sides. None of the subjects reached stages 4 or 5 of the scale. The major difference was seen in the bruising, where the left side treated with the K2 Gel showed more bruising (total score 26) than the right side (total score 13) that were treated with the XO gel. The swelling on the left side (K2, total score 12) was slightly more than on the right side (XO, total score 11), but with a difference that is too low to be conclusive.
See chart.

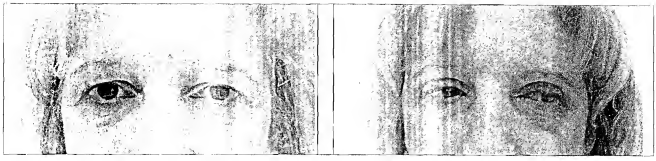
	BRUISING	SCORE	SWELLING	SCORE
PATIENT	R-XO	L-K2	R-XO	L-K2
N°1	1	2	1	2
N°2	1	2	1	1
N°3	1	3	1	1
N°4	1	2	0	0
N°5	2	3	3	2
N°6	2	3	1	1
N°7	1	3	1	1
N°8	1	3	1	1
N°9	1	2	1	1
N°10	1	3	1	2
Total	12	26	11	12

Conclusion

Even in operations known for major bruising, the downtime can be limited thanks to vitamin K preparations. The XO metabolite shows a faster resolution and is more efficient than the K2.
Further it seems to have an additional anti oedematous effect.

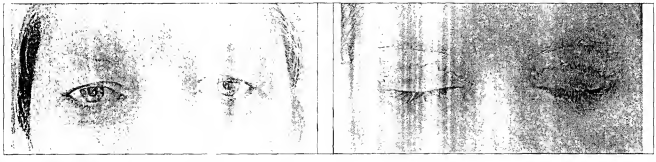
Pictures

Patient 1

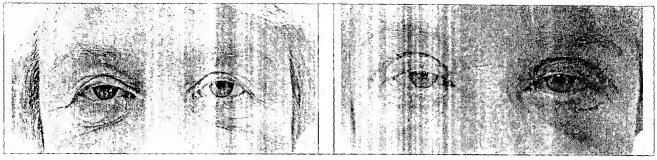


Patient 2

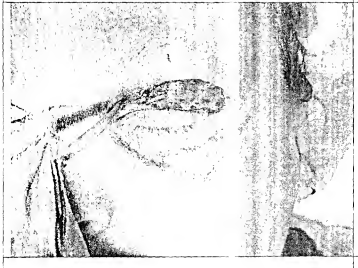
Patient 3



Patient 4



Blepharoplasty – Steps

Resection of skin	Resection of fat
	
Resection of muscle	Closure